

Please amend claim 24 as follows:

A18
24. (AMENDED) The cell surface complex of claim 23, wherein said alpha 6 subunit containing integrin-mediated signal transduction pathway modification agent is a peptide having the formula f-Met-Leu-X where X (SEQ ID NO's: 5, 3 and 6) is selected from the group consisting of Tyr, Tyr-Phe (SEQ ID NO: 5), Phe-Phe (SEQ ID NO: 3) and Phe-Tyr (SEQ ID NO: 6).

Please amend claim 26 as follows:

A19
26. (AMENDED) The method of claim 25, wherein said alpha 6 subunit containing integrin-mediated signal transduction pathway modification agent is a peptide having the formula f-Met-Leu-X where X (SEQ ID NO's: 5, 3 and 6) is selected from the group consisting of Tyr, Tyr-Phe (SEQ ID NO: 5), Phe-Phe (SEQ ID NO: 3) and Phe-Tyr (SEQ ID NO: 6).

IN THE ABSTRACT:

Please amend the Abstract as follows:

(AMENDED) ABSTRACT OF THE DISCLOSURE

A20
A method for modulating an alpha 6 subunit containing integrin-mediated signal transduction is described. The method involves contacting a cell with an effective integrin modulating amount of an alpha 6 subunit containing integrin-mediated signal transduction pathway modification agent. Preferred agents are peptides having the formula f-Met-Leu-X, wherein X (SEQ ID NO's: 5, 3 and 6) is selected from the group consisting of Tyr, Tyr-Phe (SEQ ID NO: 5), Phe-Phe (SEQ ID NO: 3) and Phe-Tyr (SEQ ID NO: 6).

REMARKS

The amendments have been made to comply with the "Notice to Comply with Requirements for Patent Applications Containing Nucleotide Sequence and/or Amino Acids Sequence Disclosures" mailed December 6, 2001, whereby, the sequences in the application are

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Application No.: 09/863,837
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identified throughout the application. These amendments introduce no new matter and their entry is respectfully requested.

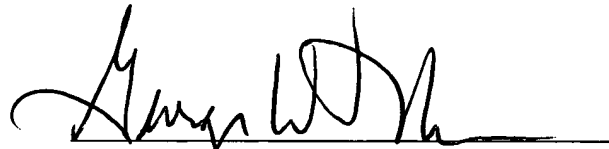
Attached hereto is a marked-up version of the changes made to the specification, claims, and Abstract, by the current amendment. The attached page is captioned:

"Version with markings to show changes made."

It is believed the application is in condition for immediate allowance, which action is earnestly solicited.

Respectfully submitted,

DATE: 21 May '02



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VERSION WITH MARKINGS TO SHOW CHANGES MADE

In the specification:

IN THE SPECIFICATION:

On page 1, lines 20 - 23, have been amended as follows:

(AMENDED) Synthetic tetrapeptides, particularly f-Met-Ile-Phe-Leu (SEQ ID NO: 1) and f-Met-Leu-Phe-Ile (SEQ ID NO: 2), have also subsequently been shown to evoke neutrophil responses (Rot et al., *Proc. Natl. Acad. Sci. USA* 84:7967-7971, 1987).

On page 2, lines 4 - 11, have been amended as follows:

(AMENDED) In particular, fMet-Leu-Phe-Phe (SEQ ID NO: 3), fMet-Leu-Phe-NHBzl (fMet-Leu-Phe benzylamide), and fNle-Leu-Phe-Tyr (N-formyl-L-norleucyl-Leu-Phe-Tyr) (Kermode et al., *Biochem. J.*, 276: 715-723, 1991) showed both maximal migration (on the order of 20-35 μ m) and degranulation (on the order of ED₅₀ of 10⁻¹⁰ to 10⁻¹¹). More recent reports suggest that nonformylated peptides may also bind to FPR and can act as potent activators of neutrophil function. For example, Met-Met-Trp-Leu-Leu (SEQ ID NO: 4) is a potent pentapeptide and is comparable in neutrophil function activity to FMLP (Chen et al., *J. Biol. Chem.* 270: 23398-23401, 1995).

On page 10, lines 9 - 15, have been amended as follows:

(AMENDED) Particularly useful peptides are those having the formula f-Met-Leu-X where X (SEQ ID NO's: 5, 3 and 6) is selected from the group consisting of Tyr, Tyr-Phe (SEQ ID NO: 5), Phe-Phe (SEQ ID NO: 3) and Phe-Tyr (SEQ ID NO: 6), most preferably f-Met-Leu-Phe-Phe (SEQ ID NO: 3). Thus, preferred embodiments of the present invention provides a complex of an $\alpha 6$ integrin subunit with a peptide having the formula f-Met-Leu-X where X (SEQ ID NOs: 5, 3 and 6) is selected from the group consisting of Tyr, Tyr-Phe (SEQ ID NO: 5),

Phe-Phe (SEQ ID NO: 3) and Phe-Tyr (SEQ ID NO: 6), most preferably f-Met-Leu-Phe-Phe (SEQ ID NO: 3).

On page 10, lines 17 - 21, have been amended as follows:

(AMENDED) In accord with the present invention, a method for treating an VLA-6 integrin-mediated pathological condition in a mammal comprises administering to the mammal an effective amount of VLA6-IMSTPMA, preferably a peptide having the formula f-Met-Leu-X where X (SEQ ID NO's: 5, 3 and 6) is selected from the groups consisting of Tyr, Tyr-Phe (SEQ ID NO: 5), Phe-Phe (SEQ ID NO: 3) and Phe-Tyr (SEQ ID NO: 6).

On page 11, lines 8 - 11, have been amended as follows:

(AMENDED) The method comprises administering to a mammal an effective VLA-6 integrin-mediated signal transduction modulating amount of VLA6-IMSTPMA, preferably a peptide having the formula f-Met-Leu-X where X (SEQ ID NO's: 5, 3 and 6) is selected from the group consisting of Tyr, Tyr-Phe (SEQ ID NO: 5), Phe-Phe (SEQ ID NO: 3) and Phe-Tyr (SEQ ID NO: 6).

On page 11, lines 15 - 22, have been amended as follows:

(AMENDED) The method comprises contacting a cell with an effective VLA-6 integrin-mediated signal transduction modulating amount of VLA6-IMSTPMA, preferably a peptide having the formula f-Met-Leu-X where X (SEQ ID NO's: 5, 3 and 6) is selected from the groups consisting of Tyr, Tyr-Phe (SEQ ID NO: 5), Phe-Phe (SEQ ID NO: 3) and Phe-Tyr (SEQ ID NO: 6). Preferably, a method for inhibiting cancer cell metastasis in a mammal comprises administering to the mammal an effective metastasis inhibiting amount of a peptide having the formula f-Met-Leu-X where X (SEQ ID NO's: 5, 3 and 6) is selected from the groups consisting of Tyr, Tyr-Phe (SEQ ID NO: 5), Phe-Phe (SEQ ID NO: 3) and Phe-Tyr (SEQ ID NO: 6).

On page 11, lines 27 - 31, , have been amended as follows:

(AMENDED) The method comprises administering to the mammal an effective VLA-6 integrin-mediated signal transduction modulating amount of VLA6-IMSTPMA, preferably a peptide having the formula f-Met-Leu-X where X (SEQ ID NO's: 5, 3 and 6) is selected from the groups consisting of Tyr, Tyr-Phe (SEQ ID NO: 5), Phe-Phe (SEQ ID NO: 3) and Phe-Tyr (SEQ ID NO: 6).

On page 12, lines 15 - 17, have been amended as follows:

(AMENDED) FIG. 1A - FIG. 1B are graphs showing the relationship between the DNA content of normal human peripheral blood mononuclear cells and the amount of fluoresceinated HK-X (f-Met-Leu-Phe-Phe) (SEQ ID NO: 3) binding to the surface of the cells.

On page 13, lines 29 - 30 through to page 14, lines 1-2, , have been amended as follows:

(AMENDED) Preferred VLA6-IMSTPMA agents are certain small peptides having the formula f-Met-Leu-X where X (SEQ ID NO's: 5, 3 and 6) is selected from the group consisting of Tyr, Tyr-Phe (SEQ ID NO: 5), Phe-Phe (SEQ ID NO: 3) and Phe-Tyr (SEQ ID NO: 6).

On page 24, lines 27 - 29, have been amended as follows:

(AMENDED) The cells were then either exposed to the 100nM FITC-labeled f-Met-Leu-Phe-Phe (SEQ ID NO: 3) (HK-X) or were exposed to a control (vehicle not containing peptide).

IN THE CLAIMS:

Claim 2 has been amended as follows:

2. (AMENDED) The method of claim 1, wherein said alpha 6 subunit containing integrin-mediated signal transduction pathway modification agent is a peptide having the formula f-Met-Leu-X where X (SEQ ID NO's: 5, 3 and 6) is selected from the group consisting of Tyr, Tyr-Phe (SEQ ID NO: 5), Phe-Phe (SEQ ID NO: 3) and Phe-Tyr (SEQ ID NO: 6), wherein said peptide is capable binding with an α_6 integrin subunit.

Claim 9 has been amended as follows:

9. (AMENDED) The method of claim 1, wherein said peptide is f-Met-Leu-Phe-Phe
(SEQ ID NO: 3).

Claim 11 has been amended as follows:

11. (AMENDED) The method of claim 10, wherein said ~~an~~ alpha 6 subunit containing integrin-mediated signal transduction pathway modification agent is a peptide having the formula f-Met-Leu-X where X (SEQ ID NO's: 5, 3 and 6) is selected from the group consisting of Tyr, Tyr-Phe (SEQ ID NO: 5), Phe-Phe (SEQ ID NO: 3) and Phe-Tyr (SEQ ID NO: 6).

Claim 14 has been amended as follows:

14. (AMENDED) The cell surface complex of claim 13, wherein said alpha 6 subunit containing integrin-mediated signal transduction pathway modification agent is a peptide having the formula f-Met-Leu-X where X (SEQ ID NO's: 5, 3 and 6) is selected from the group consisting of Tyr, Tyr-Phe (SEQ ID NO: 5), Phe-Phe (SEQ ID NO:3) and Phe-Tyr (SEQ ID NO: 6).

Claim 16 has been amended as follows:

16. (AMENDED) The method of claim 15, wherein said alpha 6 subunit containing integrin-mediated signal transduction pathway modification agent is a peptide having the formula f-Met-Leu-X where X (SEQ ID NO's: 5, 3 and 6) is selected from the group consisting of Tyr, Tyr-Phe (SEQ ID NO: 5), Phe-Phe (SEQ ID NO: 3) and Phe-Tyr (SEQ ID NO: 6).

Claim 19 has been amended as follows:

19. (AMENDED) The cell surface complex of claim 18, wherein said alpha 6 subunit containing integrin-mediated signal transduction pathway modification agent is a peptide having the formula f-Met-Leu-X where X (SEQ ID NO's: 5, 3 and 6) is selected from the group

consisting of Tyr, Tyr-Phe (SEQ ID NO: 5), Phe-Phe (SEQ ID NO: 3) and Phe-Tyr (SEQ ID NO: 6).

Claim 21 has been amended as follows:

21. (AMENDED) The method of claim 20, wherein said alpha 6 subunit containing integrin-mediated signal transduction pathway modification agent is a peptide having the formula f-Met-Leu-X where X (SEQ ID NO's: 5, 3 and 6) is selected from the group consisting of Tyr, Tyr-Phe (SEQ ID NO: 5), Phe-Phe (SEQ ID NO: 3) and Phe-Tyr (SEQ ID NO: 6).

Claim 24 has been amended as follows:

24. (AMENDED) The cell surface complex of claim 23, wherein said alpha 6 subunit containing integrin-mediated signal transduction pathway modification agent is a peptide having the formula f-Met-Leu-X where X (SEQ ID NO's: 5, 3 and 6) is selected from the group consisting of Tyr, Tyr-Phe (SEQ ID NO: 5), Phe-Phe (SEQ ID NO: 3) and Phe-Tyr (SEQ ID NO: 6).

Claim 26 has been amended as follows:

26. (AMENDED) The method of claim 25, wherein said alpha 6 subunit containing integrin-mediated signal transduction pathway modification agent is a peptide having the formula f-Met-Leu-X where X (SEQ ID NO's: 5, 3 and 6) is selected from the group consisting of Tyr, Tyr-Phe (SEQ ID NO: 5), Phe-Phe (SEQ ID NO: 3) and Phe-Tyr (SEQ ID NO: 6).

IN THE ABSTRACT:

The Abstract has been amended as follows:

(AMENDED) ABSTRACT OF THE DISCLOSURE

A method for modulating an alpha 6 subunit containing integrin-mediated signal transduction is described. The method involves contacting a cell with an effective integrin modulating amount of an alpha 6 subunit containing integrin-mediated signal transduction pathway modification agent. Preferred agents are peptides having the formula f-Met-Leu-X, wherein X (SEQ ID NO's: 5, 3 and 6) is selected from the group consisting of Tyr, Tyr-Phe (SEQ ID NO: 5), Phe-Phe (SEQ ID NO: 3) and Phe-Tyr (SEQ ID NO: 6).